REMARKS

Claims 1-38 were pending the application. Claims 17-35 have been cancelled as being drawn to a non-elected invention. Claims 1-16 and 36-38 have also been cancelled, without prejudice. Claims 39-54 have been added. Accordingly, upon entry of this amendment, claims 39-54 will be pending.

Support for the new claims may be found, at least, in the specification and claims as originally filed. In particular, support for claim 50 may be found at, for example, page 26, line 29 of Applicants' specification. Support for claims 43 and 44 may be found at, for example, Table 1 of Applicants' specification.

No new matter has been added. Any amendments to and/or cancellation of the claims should in no way be construed as an acquiescence to any of the Examiner's rejections and was done solely to more particularly point out and distinctly claim the subject matter of Applicants' invention in order to expedite the prosecution of the application. Applicants reserve the right to pursue the claims as originally filed in this or a separate application(s).

Rejection of Claims 1-16 and 36-38 Under 35 U.S.C. §101

The Examiner has rejected claims 1-16 and 36-38 under 35 U.S.C. 101 because "the claimed invention lacks credible utility."

Applicants have canceled claims 1-16 and 36-38, thus rendering the instant rejection moot as it pertains to these claims. With respect to claims 39-54, Applicants respectfully traverse the foregoing rejection and assert that a specific, substantial and well-established utility, which would have been credible to one skilled in the art at the time of the invention, is clearly disclosed in the instant specification.

Claims 39 and 40 are directed to an isolated nucleic acid molecule comprising or consisting of the nucleotide sequence of SEQ ID NO:1, or a complement thereof. Claims 41 and 42 are directed to an isolated nucleic acid molecule which encodes a polypeptide comprising or consisting of the amino acid sequence of SEQ ID NO:2, or a complement thereof. Claims 43 and 44 are directed to an isolated nucleic acid molecule comprising or

consisting of a nucleotide sequence which is at least 90% identical to the nucleotide sequence of SEQ ID NO:1, or a complement thereof, wherein said nucleotide sequence encodes a polypeptide which is capable of functioning as a phosphate transport ATP-binding protein. Claim 45 is directed to an isolated nucleic acid molecule comprising a fragment of at least 50 nucleotides of the nucleotide sequence of SEQ ID NO:1, or a complement thereof. Dependent claims 46-52 are directed to vectors and host cells containing the nucleic acid molecules of claims 39-45. Dependent claim 53 is directed to a host cell comprising the nucleic acid molecule of claim 39, wherein the nucleic acid molecule is disrupted, and dependent claim 54 is directed to a host cell comprising the nucleic acid molecule of claim 39, wherein the regulatory region of the nucleic acid molecule is modified relative to the wild-type regulatory region of the molecule.

As stated by the Examiner, "[t]he cited utilities in the specification include modulation of chemical production and using the proteins to produce fine chemicals. ***These utilities are credible***." Applicants' respectfully submit that Applicants asserted utilities are also specific and substantial. The molecules described in Applicants' specification are membrane construction and membrane transport (MCT) polypeptides. In particular, SEQ ID NO:1 encodes a phosphate transport ATP-binding protein (see Table 1 of Applicants' specification). The claimed polynucleotides and polypeptides, *e.g.,* the sequences of SEQ ID NO:1 and SEQ ID NO:2, have phosphate transport ATP-binding protein activity as described in the instant application. Applicants have described the chemical, physical and the functional characteristics of the MCT polypeptides, *e.g.,* the phosphate transport ATP-binding polypeptides of the invention, in the instant specification, including, for example, page 8, lines 18-30, page 17, line 25 through page 20, line 19, page 44, line 2 through page 47, line 34, and in Table 1.

Furthermore, the specification teaches the activities of the MCT polypeptides at, for example, page 8, line 20-29, as set forth below:

> [t]he molecules of the invention may be utilized in the modulation of production of fine chemicals from microorganisms, such as *C. glutamicum*, either directly (*e.g.*, where overexpression or optimization of a fatty acid biosynthesis protein has a direct impact on the yield,

> production, and/or efficiency of production of the fatty acid from modified *C. glutamicum*), or may have an indirect impact which nonetheless results in an increase of yield, production, and/or efficiency of production of the desired compound (*e.g.*, where modulation of the metabolism of cell membrane components results in alterations in the yield, production, and/or efficiency of production or the composition of the cell membrane, which in turn may impact the production of one or more fine chemicals).

As the Examiner is aware, the applicant does not have to provide evidence sufficient to establish that an asserted utility is true "beyond reasonable doubt." *In re Irons*, 340 F.2d 974, 978, 144 USPQ 351, 354 (CCPA 1965). Instead, evidence will be sufficient, if considered as a whole, it leads a person of ordinary skill in the art to conclude that the asserted utility is more likely than not true. M.P.E.P. §2164.07. Based on the teachings in Applicants' specification regarding the activity of the molecules used in the methods of the invention, Applicants respectfully submit that a person of ordinary skill in the art would conclude that Applicants' asserted utility is more likely than not true, which is all that is required under 35 U.S.C. §101.

In view of the foregoing, Applicants asserts that the utilities set forth in the specification for the invention as instantly claimed are specific, credible and substantial and/or well-established utilities that would have been recognized as such by one of skill in the art at the time the application was filed. Therefore, the instant claims meet the requirements of 35 U.S.C. §101, and Applicants respectfully request reconsideration and withdrawal of this rejection.

Rejection of Claims 1-16 and 36-38 Under 35 U.S.C. §112, First Paragraph

The Examiner has rejected claims 1-16 and 36-38 under 35 U.S.C. 112, first paragraph "as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention." In particular, the Examiner is of the opinion that "[a]ll of the current claims encompass a genus of nucleic acids which are different from those disclosed in the specification, since

the claims are not limited to any particular SEQ ID NO, but are open to a nucleic acid which encodes any protein named MCT, without any structure whatsoever provided."

Applicants have canceled claims 1-16 and 36-38, thus rendering the instant rejection moot as it pertains to these claims. With respect to claims 39-54, Applicants respectfully traverse the foregoing rejection and submit that there is sufficient written description in Applicants' specification regarding nucleic acid molecules comprising SEQ ID NO:1, nucleic acid molecules with a significant degree of homology to SEQ ID NO:1 and SEQ ID NO:2, and nucleic acids which encode polypeptides which are capable of functioning as phosphate transport ATP-binding proteins, to inform a skilled artisan that Applicants were in possession of the claimed invention at the time the application was filed as required by section 112, first paragraph (see M.P.E.P. 2163.02). In order to meet the written description requirement of the first paragraph of 35 U.S.C. §112, it is not necessary that a patent specification describe each and every specific member of a genus recited in a claim.

With respect to claims 39-54, a claim to a genus of chemical compounds satisfies the written description requirement when its accompanying specification either defines by sequence a representative number of its members falling within the scope of the genus or when its accompanying specification defines the structural features common to a substantial portion of the genus *(The Regents of the University of California v. Eli Lilly and Co.*, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997)). For reasons discussed in detail below, the instant specification satisfies this requirement for the claimed invention.

The instant specification describes how modified or disrupted variants of SEQ ID NO:1 may be identified or produced (see, for example, page 38, lines 8-19), and teaches what kind of sequence variation functional and non-functional variants of a polypeptide encoded by SEQ ID NO:1 may have (see, for example, page 27, lines 9-21).

Example 14 of the *Revised Interim Written Description Guidelines Training Materials* provides that a claim directed to variants of a polypeptide having SEQ ID NO:3 "that are at least 95% identical to SEQ ID NO:3 and catalyze the reaction of A→B" with an accompanying specification that discloses a single species falling within the claimed genus, satisfies the requirements of 35 U.S.C. §112, first paragraph for written

description. The rationale behind the foregoing conclusion, as presented by the *Written Description Guidelines*, is that "[t]he single species disclosed is representative of the genus because all members have at least 95% structural identity with the reference compound and because of the presence of an assay which Applicant provided for identifying all of the at least 95% identical variants of SEQ ID NO:3 which are capable of the specified catalytic activity."

Similarly, in the present case, claims 43-44 are directed to isolated nucleic acid molecules comprising or consisting of a nucleotide sequence that is at least 90% identical to the nucleotide sequence shown in SEQ ID NO:1, wherein the nucleotide sequence encodes a polypeptide capable of functioning as a phosphate transport ATP-binding protein.

Applicants have disclosed in the instant specification assays for identifying all of the at least 90% identical variants of SEQ ID NO:1 which encode polypeptides capable of functioning as a phosphate transport ATP-binding protein (see, for example, page 51, line 18 through page 55, line 24 of the specification). Thus, based on the teachings in Applicants' specification, one of skill in the art would conclude that Applicants were in possession of the claimed invention at the time of filing.

With respect to claim 45, which is directed to an isolated nucleic acid molecule which encodes a polynucleotide fragment comprising at least 50 contiguous nucleic acid residues of the amino acid sequence of SEQ ID NO:1, Applicants have described various fragments of the polynucleotides of the invention.

In Example 15 of the *Interim Guidelines for Examination of Patent Applications Under the 35 U.S.C. §112, First Paragraph Written Description Requirement* the "theoretical specification" discloses a messenger RNA sequence, SEQ ID NO:1, which encodes a human growth hormone. The "theoretical specification" claims antisense molecules that inhibit the production of human growth hormone. The Guidelines provide that

> [c]onsidering the specification's disclosure of (1) ***the sequence (SEQ ID NO:1) which defines and limits the structure of any effective molecules such that one skilled in the art would be able to immediately envisage members of the genus embraced by the claim*** and 2) the functional characteristics of the claimed invention as well as a routine art-recognized

> method of screening for antisense molecules which provide further distinguishing characteristics of the claimed invention, along with, 3) the general level of knowledge and skill in the art, one skilled in the art would conclude that applicant was in possession of the invention.....***the claimed invention is adequately described.***

Similar to Example 15 of the *Interim Guidelines*, the instant specification describes the nucleotide sequence of the nucleic acid molecules of the invention (SEQ ID NO:1) ***which define and limit the structure of any nucleotide fragments such that one skilled in the art would be able to immediately envisage members of the genus embraced by the nucleotide fragment claims***.

Moreover, as provided in Example 15 of the *Interim Guidelines*, the generation of oligonucleotide fragments is routine. For example, (as indicated in Example 15 of the *Interim Guidelines*) any specified fragment can be ordered from a commercial synthesizing service. Finally, Applicants' specification teaches how such polynucleotide fragments encoding polypeptides may be tested for activity (see, for example, page 40, line 36 through page 41, line 11 of Applicants' specification).

Based on the foregoing teachings in Applicants' specification and the knowledge generally available in the art, one skilled in the art would conclude that Applicants were in possession of the claimed invention at the time of filing of the application. The skilled artisan would also be able to make and use the claimed polypeptide fragments using only routine experimentation.

Accordingly, based on the amendments to the claims and the comments set forth above, Applicants respectfully request reconsideration and withdrawal of the instant rejection under 35 U.S.C. § 112, first paragraph.

Rejection of Claims 1-16 and 36-38 Under 35 U.S.C. §112, First Paragraph

The Examiner has rejected claims 1-16 and 36-38 under 35 U.S.C. 112, first paragraph "as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention." In particular, the Examiner is of the opinion that

> given the broad claims in an art whose nature is identified as unpredictable, the unpredictability of the art, the large quantity of research required to define these unpredictable variables, the lack of guidance provided in the specification, the presence of a working example which does not address the issue of the efficacy of the control and the negative teachings in the prior art balanced only against the high skill level in the art, it is the position of the examiner that it would require undue experimentation for one of skill in the art to perform the ***method of the claim*** as broadly written. (***Emphasis added***).

Applicants have canceled claims 1-16 and 36-38, thus rendering the instant rejection moot as it pertains to these claims. With respect to claims 39-54, Applicants respectfully traverse the foregoing rejection and submit that the pending claims are fully enabled by Applicants' specification.

Claims 39 and 40 are directed to an isolated nucleic acid molecule comprising or consisting of the nucleotide sequence of SEQ ID NO:1, or a complement thereof. Claims 41 and 42 are directed to an isolated nucleic acid molecule which encodes a polypeptide comprising or consisting of the amino acid sequence of SEQ ID NO:2, or a complement thereof. Claims 43 and 44 are directed to an isolated nucleic acid molecule comprising or consisting of a nucleotide sequence which is at least 90% identical to the nucleotide sequence of SEQ ID NO:1, or a complement thereof, wherein said nucleotide sequence encodes a polypeptide which is capable of functioning as a phosphate transport ATP-binding protein. Claim 45 is directed to an isolated nucleic acid molecule comprising a fragment of at least 50 contiguous nucleotides of the nucleotide sequence of SEQ ID NO:1, or a complement thereof. . Dependent claims 46-52 are directed to vectors and host cells containing the nucleic acid molecules of claims 39-45. Dependent claim 53 is directed to a host cell comprising the nucleic acid molecule of claim 39, wherein the nucleic acid molecule is disrupted, and dependent claim 54 is directed to a host cell comprising the nucleic acid molecule of claim 39, wherein the regulatory region of the nucleic acid molecule is modified relative to the wild-type regulatory region of the molecule.

Contrary to the Examiner's assertions, the instant claims are directed to specification nucleic acid molecules, rather than methods.

Applicants respectfully direct the Examiner's attention to Example 14 of the *Revised Interim Written Description Guidelines Training Materials*, which provides that a claim directed to variants of a protein having SEQ ID NO:3 "that are at least 95% identical to SEQ ID NO:3 and catalyze the reaction of A→B" with an accompanying specification that discloses a single species falling within the claimed genus, satisfies the requirements of 35 U.S.C. §112, first paragraph for written description. The rationale behind the foregoing conclusion, as presented by the *Written Description Guidelines*, is that "[t]he single species disclosed is representative of the genus because all members have at least 95% structural identity with the reference compound and because of the presence of an assay which Applicant provided for identifying all of the at least 95% identical variants of SEQ ID NO:3 which are capable of the specified catalytic activity." The Guidelines also provide that "***[t]he procedures for making variants of SEQ ID NO:3 are conventional in the art and an assay is described which will identify other proteins having the claimed catalytic activity. Moreover, procedures for making variants of SEQ ID NO:3 which have 95% identity to SEQ ID NO:3 and retain its activity are conventional in the art.***"

As set forth in Example 14 of the Written Description Guidelines, procedures for making variants of SEQ ID NO:3 which have 95% identity to SEQ ID NO:3 and retain its activity are conventional in the art." Furthermore, Applicants have disclosed in the instant specification assays for identifying all of the at least 90% identical variants of SEQ ID NO:1 which encode proteins capable of functioning as a phosphate transport ATP-binding protein (see, for example, page 51, line 18 through page 55, line 24 of the specification). Phosphate transport ATP-binding protein activity is readily testable by one of skill in the art by the methods described in the specification and by methods well-known in the relevant art. Accordingly, it would require only routine experimentation on the part of one of skill in the art to mutate the molecules of the invention and test them for phosphate transport ATP-binding protein activity.

With respect to the Wands factors cited by the Examiner, applicants wish to make the following of record:

The claimed invention is directed to SEQ ID NO:1, nucleic acid molecules with a significant degree of homology to SEQ ID NO:1, *i.e.,* 90% homology, which encode a polypeptide which is capable of functioning as a phosphate transport ATP-binding proteins, as well as specific fragments of SEQ ID NO:1. The nucleic acid molecules of the invention are sufficiently described by Applicants' specification to enable one of ordinary skill in the art to make and use the claimed invention without undue experimentation. Therefore, the claims are fully enabled across their breadth.

Furthermore, the art of sequencing isolated nucleic acid molecules is relatively predictable. Moreover, as set forth above, Applicants' specification provides specific, substantial, and credible uses for the nucleic acid molecules of the invention.

Applicants respectfully submit that "[t]he specification need not contain an example if the invention is otherwise disclosed in such manner that one skilled in the art will be able to practice it without an undue amount of experimentation." (M.P.E.P. §2164.02; *In re Borkowski*, 422 F.2d 904, 908, 164 USPQ 642, 645 (CCPA 1970). Applicants' specification provides detailed disclosure regarding the nucleic acid molecules of the invention. Accordingly, Applicants' specification provides sufficient disclosure such that one or ordinary skill in the art would be able to practice the methods of the invention without undue experimentation.

In order for a claimed invention to be enabled, the standard is not whether or not experimentation is necessary to practice the claimed invention. Rather, the standard is whether or not the experimentation necessary to practice the claimed invention is undue (See *In re Wands*, 858 F.2d at 737). Thus, enablement is not precluded by the necessity for some experimentation, and a considerable amount of experimentation is permitted. *In re Wands*, supra. As set forth above, Applicants provide sufficient guidance such that one of ordinary skill in the art could practice the claimed invention without undue experimentation. Accordingly, Applicants submit that the claimed invention is fully enabled by the disclosure in Applicants' specification and respectfully request that the Examiner reconsider and withdraw the foregoing rejection.

Rejection of Claims 1-8, 10-13, 15, 16, and 37 Under 35 U.S.C. §102(b)

The Examiner has rejected claims1-8, 10-13, 15, 16, and 37 under 35 U.S.C. 102(b) "as being anticipated by Genbank Accession Number AF045938 (02 May 1998)." In particular, the Examiner is of the opinion that

> Genbank AF045938 teaches a nucleic acid sequence which encodes an ABC transporter gene which has 74% local similarity with SEQ ID NO:1 and which would hybridize to SEQ ID NO:1 under stringent conditions. Genbank AF045938 comprises many portions of SEQ ID NO:1, including, for example, the 17 mer from nucleotides 123 to 140 of SEQ ID NO:1. Genbank AF045938 teaches the sequence in a Mycobacterium host cell in the genome, which permits expression of the protein and which is modified. Genbank AF045938 inherently is involved in the production of chemicals in the cell which are organic in nature. Lastly, Genbank AF04593 inherently has one or more modifications from the sequence set forth in Appendix A.

Applicants have canceled claims 1-8, 10-13, 15, 16, and 37, thus rendering the instant rejection moot as it pertains to these claims. With respect to claims 39-54, Applicants respectfully traverse the foregoing rejection.

Applicant respectfully traverses the foregoing rejection. Applicant respectfully submits that for a prior art reference to anticipate in terms of 35 U.S.C. §102 a claimed invention, prior art must teach ***each and every element*** of the claimed invention. Lewmar Marine v. Barient 827 F.2d 744, 3 USPQ2d 1766 (Fed. Cir. 1987).

Claims 39 and 40 are directed to an isolated nucleic acid molecule comprising or consisting of the nucleotide sequence of SEQ ID NO:1, or a complement thereof. Claims 41 and 42 are directed to an isolated nucleic acid molecule which encodes a polypeptide comprising or consisting of the amino acid sequence of SEQ ID NO:2, or a complement thereof. Claims 43 and 44 are directed to an isolated nucleic acid molecule comprising or consisting of a nucleotide sequence which is ***at least 90% identical*** to the nucleotide sequence of SEQ ID NO:1, or a complement thereof, wherein said nucleotide sequence encodes a polypeptide which is capable of functioning as a phosphate transport ATP-binding protein. Claim 45 is directed to an isolated nucleic acid molecule comprising a fragment of ***at least 50 continuous nucleotides*** of the nucleotide sequence of SEQ ID NO:1, or a complement thereof.

Genbank Accession Number AF045938 discloses a Mycobacterium smegmatis putative ABC transporter nucleotide binding subunit (mtp1) gene. Genbank Accession Number AF045938 clearly does not teach or suggest SEQ ID NO:1. Furthermore, as shown in the alignment provided by the Examiner, Genbank Accession Number AF045938 has a best local similarity of 74.2% to SEQ ID NO:1. Accordingly, Genbank Accession Number AF045938 does not teach or suggest the isolated nucleic acid molecules of claims 43 or 44. Moreover, Genbank Accession Number AF045938 does not teach or suggest an isolated nucleic acid molecule comprising a fragment of at least 50 continuous nucleotides of the nucleotide sequence of SEQ ID NO:1, as set forth in claim 45.

Furthermore, Applicants respectfully submit that claims 46-54 are dependent upon claims 39-45. As set forth above, Genebank AF045938 fails to teach or suggest each and every element of claims 39-45, and therefore fails to teach each and every element of claims 46-54.

Therefore, for the reasons set forth above, Genbank Accession Number AF045938 fails to teach each and every element of the claimed invention. Accordingly, Applicants respectfully request reconsideration and withdrawal of the instant rejection.

Rejection of Claims 9, 14, 36, and 38 Under 35 U.S.C. §103(a)

The Examiner has rejected claims 9, 14, 16, and 38 under 35 U.S.C. 103(a). In particular, the Examiner is of the opinion that

> Genebank AF045938 does not expressly teach placing the nucleic acid molecule in a vector with a heterologous polypeptide, expressing in Corynebacterium, disrupting the nucleic acid, or using a heterologous regulatory region. Ago teaches expression of a bacterium protein in vectors such as pBTac2 and pBTrp2 and pBluescript (see column 5, lines 11-16), each of which places the nucleic acid under the control of a heterologous regulatory region and in a vector with a heterologous polypeptide such as an antibiotic resistance gene. Further Ago teaches expression in Corynebacterium and Brevibacterium (see column 4, lines 56-60). Lastly, Ago teaches disruption of nucleic acids to alter the expression level of the gene (see column 4, lines 35-38).

Applicants respectfully traverse the foregoing rejection. For a prior art reference (or references when combined) to render an application obvious, the prior art reference (or references when combined) must teach or suggest all the claim limitations (M.P.E.P. 2143).

Applicants have canceled claims 9, 14, 16, and 38, thus rendering the instant rejection moot as it pertains to these claims. With respect to claims 39-54, Applicants respectfully traverse the foregoing rejection.

As set forth above, Genebank AF045938 fails to teach or suggest the nucleic acid molecule of SEQ ID NO:1, an isolated nucleic acid molecule comprising or consisting of a nucleotide sequence which is at least 90% identical to the nucleotide sequence of SEQ ID NO:1, or a complement thereof, wherein said nucleotide sequence encodes a polypeptide which is capable of functioning as a phosphate transport ATP-binding protein, or an isolated nucleic acid molecule comprising a fragment of at least 50 continuous nucleotides of the nucleotide sequence of SEQ ID NO:1, or a complement thereof, as is set forth in claims 39-45.

Ago, *et al.* (USPN 5,955,137) discloses polypeptide (set forth as SEQ ID NO:1) having ferulic acid decarboxylase activity, a gene encoding the protein, a recombinant

vector comprising the gene, a transformant carrying the recombinant vector, and a process for producing 4-vinylguaiacol, vanillin or vanillic acid, or a distilled liquor.

Ago, *et al.* fails to cure the deficiencies of Genebank AF045938 as it does not teach or suggest SEQ ID NO:1, an isolated nucleic acid molecule comprising or consisting of a nucleotide sequence which is at least 90% identical to the nucleotide sequence of SEQ ID NO:1, or a complement thereof, wherein said nucleotide sequence encodes a polypeptide which is capable of functioning as a phosphate transport ATP-binding protein, or an isolated nucleic acid molecule comprising a fragment of at least 50 continuous nucleotides of the nucleotide sequence of SEQ ID NO:1, or a complement thereof.

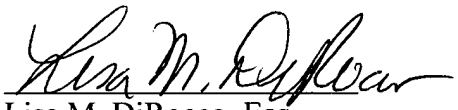
Furthermore, Applicants respectfully submit that claims 46-52 are dependent upon claims 39-45. As set forth above, the combination of Genebank AF045938 and Ago *et al.* fail to teach or suggest each and every element of claims 39-45, and therefore fail to teach each and every element of claims 46-52.

In view of the foregoing, Applicants respectfully submit that the combination of Genebank AF045938 in view of Ago, fail to teach or suggest Applicants' invention.

SUMMARY

If a telephone conversation with Applicants' Attorney would expedite the prosecution of the above-identified application, the examiner is urged to call the undersigned at (617) 227-7400.

Respectfully submitted,



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